



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of Vilmos Kéri et al.

FWCIP of Serial No. 08/659,961

Filed on herewith

For PROCESS FOR THE ISOLATION AND PURIFICATION, etc.

Attorney's Docket 0100-004

Hon. Commissioner of Patents and Trademarks
Washington DC 20231

Sir:

PRELIMINARY AMENDMENT

Prior to assigning a Serial No to the above-identified application,
please amend it as follows:

In the disclosure

Page 1, before line 1 insert This is a continuation-in-part of application Ser.
No.08/659,961 filed on June 7, 1996, which is a continuing application of Ser. No.
08/269,150 filed on June 30, 1994, both abandoned.--

Page 3, line 5, after "Collection)" insert and other bacterial strains, such as
Aspergillus terreus) accessible under ATCC 20542).

Page 14, after the end of the page add the following new Examples:

Example 7.

800 g fermentation liquor cultured by an *Aspergillus terreus* strain
(deposition access No. ATCC 20542) containing a total amount of 630 mg of
mevinolin both as lactone and as hydroxy acid were diluted to 1,200 g. with water.
Then 2.4 g ethylene glycol were added to the mixture, and the pH was main-
tained at 9 to 9.5 by adding 20% wt. KOH solution under continuous stirring for

2 hours. The biomass was then filtered off and suspended in 400 cm³ water. The suspension was adjusted to pH 9-9.5 with 20% wt. KOH solution, filtered again and the filtrates were combined. 1,480 cm³ of filtered liquor containing 554 mg of active ingredient were obtained. Then 3.5 g of CaCl₂ were added to the liquor and the solution was adjusted to pH 2.1 with 15% wt. sulfuric acid solution under stirring. The separate precipitate was settled for 4 hours and processing was completed as in Example 2, with the difference that the active ingredient was dissolved from the precipitate with 120 cm³ of isobutylacetate. 370 mg product was obtained. The obtained mevinolin has an active ingredient content of 98% by high pressure liquid chromatography, containing 0.2% dihydromevinolin by HPLC. $[\alpha]_{25_D}^{25} = +326^\circ\text{C}$ (c=0.5; acetonitrile).

A3
concl.

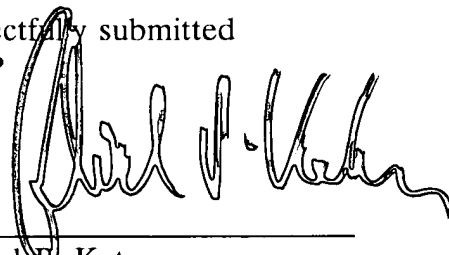
Example 8.

800 g of fermentation liquor cultured by an *Aspergillus terreus* strain and containing a total amount of 620 mg of mevinolin, both as a lactone and as hydroxy acid were diluted to 1200 g with water. Then 2.4 ethylene glycol were added to the mixture, and the pH was maintained at 8.5 to 9.0 by adding 20% wt. KOH solution under continuous stirring for 2 hours. The biomass was then filtered off and suspended in 400 cm³ water containing 0.8 g of ethylene glycol. The suspension was adjusted to pH 8.5-9.0 with 20% wt. KOH solution, filtered again and the filtrates were combined. 1,470 cm³ of filtered liquor containing 535 mg of the active ingredient were obtained which was adjusted to pH 3.0 with 15% wt. phosphoric acid under stirring. The precipitate was settled over 4 hours. The balance of the process was completed as described in Example 2, resulting in the isolation of 334 mg mevinolin with an active ingredient content of 98.6% by high pressure liquid chromatography, with a dihydromevinolin content of 0.2 % by HPLC. $[\alpha]_{25_D}^{25} = +328^\circ\text{C}$ (c=0.5; acetonitrile).--

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Respectfully submitted



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